EDITORIALS

Alcoholic Hypoglycemia and Ketosis

PLATIA AND HSU'S ARTICLE in this issue is an apt reminder that ketosis and hypoglycemia may develop in chronic alcohol abusers who are not diabetic.[1,2] Although Platia and Hsu's five patients had ketosis *and* hypoglycemia, the two abnormalities may occur separately in alcohol abusers. Indeed, in one of Miller's patients, who was admitted seven times with alcoholic ketoacidosis, there were initial serum glucose concentrations as low as 24 mg per dl and as high as 195.[3] It is not clear why just ketosis develops in some patients, just hypoglycemia in others and both in still others. Although some patients have had impaired liver function, that has not seemed to be essential in the pathogenesis of either the ketosis or hypoglycemia. Most of the patients have allegedly discontinued or severely curtailed their alcohol intake for several days before admission (and in some there has been no ethanol detectable in the blood). They have usually also stopped eating, because of anorexia, nausea, vomiting and severe abdominal pain. Indeed, acute starvation may be a major factor in the pathogenesis of both ketosis and hypoglycemia.

β-Hydroxybutyrate seems elevated disproportionately to acetoacetate, and the nitroprusside reaction has sometimes been only weakly positive (or even negative) despite considerably elevated β-hydroxybutyrate.[4,5] It is not known why β-hydroxybutyrate predominates so much over acetoacetate in this syndrome, in ratios even higher than in diabetic ketoacidosis, but coexisting lactic acidosis is apparently not the explanation. When ethanol is infused into starved rats' livers, the ratio of β-hydroxybutyrate to acetoacetate rises in the effluent.[6] However, most of the alcoholic ketotic patients apparently no longer have ethanol in their tissues. If the serum nitroprusside reaction is weakly positive or negative in a patient with an *increased-anion-gap metabolic acidosis* without uremia, the acidosis is difficult to ascribe to ketosis unless serum β-hydroxybutyrate can be rapidly measured and found elevated. Fortunately, whether such an *anion-gap-acidosis* is due to excess lactic acid, β-hydroxybutyric acid or some other unmeasured organic acid, need not alter the initial treatment with intravenously given fluid. Few patients with any of those types of metabolic acidosis will be harmed by intravenous administration of glucose solution, and some will be benefited, certainly so if they are also hypoglycemic. Of course, emergency care of such patients must include a search for specifically treatable causes of lactic acidosis, notably those due to hypovolemia and hypoperfusion.

The significance of the clinical and biochemical differences that have been noted in various series of alcoholic ketotics is difficult to judge because most of the series have been small. The differences are worth mentioning, however, because they may stimulate ideas about pathogenesis. Women have predominated in most of the series, but not in Platia and Hsu's nor in ours. Lactic acidosis, when present, has usually been due to incidentally coexisting hypoperfusion states, or occasionally acute alcoholic intoxication, and is not an essential feature of the syndrome. Blood pH has usually been low, except in our own series where many of the patients were not very acidemic (and some even alkalemic) owing to coexisting respiratory alkalosis (sometimes associated with delirium tremens), metabolic alkalosis (secondary to vomiting), or both.[5]

Alcoholic hypoglycemia seems mainly due to starvation, absent liver glycogen stores and impaired hepatic gluconeogenesis, although the explanation for the last remains unclear.[7] A conjecture that can be added to those previously suggested relates to the presumed inhibition of pyruvate dehydrogenase induced by starvation.[8,9] The consequent accumulation of pyruvate might promote conversion of glyceraldehyde-3-phosphate to diphosphoglycerate, thereby inhibiting gluconeogenesis. The pathogenesis of alcoholic ketosis is even less clear, most authors ascribing it to excess lipolytic factors (such as cortisol or growth hormone), or abnormalities of hepatic mitochondria. Serum cortisol concentrations have

often been elevated in the few patients with reported values, but cortisol is elevated in many seriously ill patients who are not ketotic. Although ethanol causes structural hepatic mitochondrial abnormalities,[10] if those abnormalities cause ketosis, why should the ketosis disappear so quickly after glucose administration? The mitochondrial structural abnormalities presumably do not. In nearly all the reported cases the patients have severely curtailed their food intake, usually for at least several days. Such starvation, superimposed on chronic malnutrition, together with the ketogenic effect of ethanol,[11] may be important in the pathogenesis of the ketosis (and the hypoglycemia). If that were the whole story, however, why do we not see more alcohol abusers with these syndromes? Perhaps the abnormalities are more common than we realize, but disappear when patients stop drinking, if only long enough to eat sufficient carbohydrate.

Treating the basic disorder—chronic alcohol abuse—is not very successful. The treatment of the hypoglycemia and ketosis, however, is; both respond rapidly to administration of glucose. Patients who are dehydrated, as many are because of vomiting, should also receive parenteral sodium chloride solutions, which may also promote the renal excretion of β-hydroxybutyrate and acetoacetate. Some patients, especially those with severe vomiting, may also require administration of potassium salts after renal function has been shown to be adequate. Whether some patients should also receive phosphate, especially because starved alcoholics may be phosphate-depleted and profound hypophosphatemia may develop during treatment (although initially they may have *hyper*phosphatemia), has been discussed by Miller and colleagues.[3]

Alcoholic ketosis is defined as a syndrome occurring in nondiabetic persons. However, having diabetes mellitus surely does not protect a vomiting, starved chronic alcoholic from ketosis. Therefore, if a patient with presumed alcoholic ketosis is also diabetic—or if not known to be diabetic, develops severe hyperglycemia during treatment with glucose—it may be prudent to administer small doses of insulin to mitigate such hyperglycemia.

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Nationalized Health Care—A Juggernaut in 1981

WEBSTER DEFINES a juggernaut as "a massive inexorable force or object that crushes whatever is in its path." Some very recent events raise the possibility of a federal juggernaut for nationalized health care in 1981. If the person elected as President in 1980 rides the crest of an emotional wave of frustration with the present and of nostalgia for the past, and if that President were to have had a long experience in Congress and an essentially unchangeable personal commitment to nationalized health care, there could develop a situation much like that in 1965. A *landslide* presidential victory in 1964 permitted a legislatively skillful President to get a sweeping social program in health care enacted into law on a crash basis, with very little concern being given to its fiscal or other consequences. The consequences have now become familiar. There has been an unanticipated and frightening escalation in costs, in no small part due to clumsy and bungling attempts at planning, regulation and control of the health care enterprise. In all fairness the goal of more and better care for more people has been achieved but the real dollar cost of this achievement was neither calculated nor foreseen.

The possibility of a similar scenario for 1980 and 1981 seems real. The mood of the country appears at the moment to favor fiscal restraint and reducing the cost of government. Taxes, monetary inflation, unwanted dependence on foreign oil, and the rising price and uncertain availability of gasoline and other forms of energy are